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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/998,481

11/30/2001

Francis Barany

19603/3331 (CRF  
D-2634A)

6387

7590

04/27/2005

EXAMINER

TUNG, JOYCE

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ART UNIT

PAPER NUMBER

1637

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/998,481

Applicant(s)

BARANY ET AL.

Examiner

Joyce Tung

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on interview dated 5/5/04.  
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-155 is/are pending in the application.  
4a) Of the above claim(s) 42-45 and 87-154 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1-41, 46-86 and 155 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 8/22/2002.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Based upon the interview dated May 5, 2004 that the Office will rescind second restriction upon clarification and proceed with examination, now claims 1-155 are pending. Claims 1-41, 46-86 and 155 are under examination. Claims 42-45, 87-154 are withdrawn from further consideration as non-elected group.

#### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Claims 1-41, 46-86 and 155 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a. Claims 1-41, 46-86 and 155 are vague and indefinite because of the phrase "can" in claims 1, 46 and 155. It is unclear whether or not the oligonucleotide primer hybridizes to the target nucleotide sequence for fulfilling the method. Clarification is required.
- b. Claims 1-41, 46-86 and 155 are vague and indefinite because of the phrase "substantially" in claims 1, 17, 46, 62 and 155. It is unclear what is the definition of the phrase in the specification.
- c. Claim 37 is vague and indefinite because claim 37 depends from claim 38 in that claim 38 do not further limit to the gene. Clarification is required.

#### ***Allowable Subject Matter***

3. Claims 1-41, 46-86 and 155 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

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4. The following is a statement of reasons for the indication of allowable subject matter:

Concerning claims 1-41, no prior art has been found teaching or suggesting the method for identifying a mutant nucleic acid sequence from a normal target nucleotide sequences comprising providing a sample containing normal target nucleotide sequence as well as the mutant nucleic acid sequence, performing polymerase chain reaction on normal target nucleotide sequence as well as the mutant nucleic acid sequence with two labeled oligonucleotide primers, forming heteroduplexed amplified products, nicking or cleaving the heteroduplexes products with an endonuclease which preferentially nicks or cleaves at a location one base away from mismatched base pairs, resealing the nicked heteroduplexed products, separating the products from the ligase resealing reaction mixture by size and detecting the presence of the normal target and the mutant nucleic acid sequence in the sample.

Concerning claims 46-86, no prior art has been found teaching or suggesting the method for identifying a mutant nucleic acid sequence from a normal target nucleotide sequences comprising the different steps compared with claim 1 which are providing a sample potentially containing the mutant nucleic acid sequence but not necessarily the normal target nucleic acid sequence and a standard containing the normal target nucleic acid sequence.

Concerning claim 155, no prior art has been found teaching or suggesting the method for identifying a mutant nucleic acid sequence from a normal target nucleotide sequences comprising the several additional steps compared with claims 1 and 46 which are using polymerase with 3'-5' exonuclease activity to remove several bases 3' to the nick, and using a polymerase without 3'-5' exonuclease activity and labeled dideoxyterminator to perform mini-

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sequencing reaction and detecting the presence of the normal target and the mutant nucleic acid sequence by mini-sequencing.

The closest prior art is the reference of Weghorst et al.. Weghorst et al. disclose for specifically detecting DNA mismatches between heteroduplex strands produced between wildtype and mutation. The method of Weghorst et al. applies the chemical modification of the heteroduplex with reagent that forms a covalent linkage to a mismatched nucleotide in the heteroduplex and detecting the chemically modified mismatched nucleotide. Weghorst et al. do not disclose applying the heteroduplexes, which are nicked or cleaved with endonuclease and resealed with ligase.

### **Summary**

5. No claims are allowable.

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6. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782 on Monday-Friday from 10:00 AM-6:00 PM.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using 571 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

April 13, 2005

  
GARY BENZION, PH.D.  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600